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DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/00217

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D207/09 A61K31/40 C07D295/12 A61K31/535 A61P9/06
A61P23/00 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BOIADJIEV S E ET AL: "pH-sensitive exciton chirality chromophore. Solvatochromic effects on circular dichroism spectra" TETRAHEDRON: ASYMMETRY, NL, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, vol. 7, no. 10, 1 October 1996 (1996-10-01), pages 2825-2832, XP004048370 ISSN: 0957-4166	1,2
A	US 5 506 257 A (MACLEOD BERNARD A ET AL) 9 April 1996 (1996-04-09) claim 1	1-89
A	WO 93 19056 A (UNIV BRITISH COLUMBIA) 30 September 1993 (1993-09-30)	1-89
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

19 June 2000

Date of mailing of the international search report

10. 07. 00

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

Gettins, M

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 00/00217

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 051 428 A (HORWELL DAVID C ET AL) 24 September 1991 (1991-09-24) claim 1	1-89
A	EP 0 380 063 A (WARNER LAMBERT CO) 1 August 1990 (1990-08-01) claim 1	1-89
A	DE COSTA ET AL: "Synthesis and evaluation of N-substituted cis-N-methyl-2-(1-pyrrolidiny) cyclohexyl amines as high affinity sigma receptor ligands." J.MED.CHEM., vol. 33, no. 11, 1990, pages 3100-3110, XP000910297 example 42; table III	1,2
A	EP 0 222 533 A (UPJOHN CO) 20 May 1987 (1987-05-20) claim 1	1,2
A	US 4 663 343 A (HORWELL DAVID C ET AL) 5 May 1987 (1987-05-05) claims 1,2	1-89
A	US 4 656 182 A (HORWELL DAVID) 7 April 1987 (1987-04-07) claim 1	1-89
A	US 4 598 087 A (HORWELL DAVID C) 1 July 1986 (1986-07-01) claim 1	1-89
A	US 4 179 501 A (SZMUSZKOVICZ JACOB) 18 December 1979 (1979-12-18) claim 1	1-89

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 00/00217

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/CA 00/00217

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims

11,13,15,17,19,21,23,25,27,29,31,33,35,37,39,41,43,45,47,49,51,53,55,57, 59,61,63,65,67,69,71,73,75,77,79,81,83,85 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Present claims 1 and 3-89 relate to an extremely large number of possible compounds/methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds/methods where X is a direct bond (as is found in all of the exemplified compounds)

One reason for the limitation is due to the ambiguity as to what is really claimed. It is noted, from the description, but not the claims, that aryl is not meant to have the standard meaning given to it by IUPAC. Not only are non standard meanings (e.g. heteroaromatic) intended, but also the term "optionally substituted" with no limitation as to the type and amount of substitution. The term "optionally substituted" is not allowed for the reasons given in the first 2 sentences of this paragraph. It is further noted that there are no examples of "aryl" being other than phenyl. On page 13, line 22 naphthyl is also referred to which falls within the classic definition of aryl. Accordingly aryl has been understood to only refer to phenyl and naphthyl.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 00/00217

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5506257	A	09-04-1996	AT 154934 T AU 3882793 A CA 2132841 A WO 9319056 A DE 69311896 D DE 69311896 T EP 0632806 A ES 2104142 T HK 1000684 A JP 7505151 T	15-07-1997 21-10-1993 30-09-1993 30-09-1993 07-08-1997 16-10-1997 11-01-1995 01-10-1997 17-04-1998 08-06-1995
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EP 0222533	A	20-05-1987	AT 49502 T DE 3668268 D EP 0248824 A GR 3000408 T JP 63501152 T US 4801604 A WO 8702584 A	15-02-1990 22-02-1990 16-12-1987 28-06-1991 28-04-1988 31-01-1989 07-05-1987
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 00/00217

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		PT 79629 A, B	01-01-1985
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		JP 1380696 C	28-05-1987
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 00/00217

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4179501 A		US 4192885 A	11-03-1980
		US 4152459 A	01-05-1979
		US 4197308 A	08-04-1980
		US 4148914 A	10-04-1979
		US 4153717 A	08-05-1979
		ZA 7706240 A	26-07-1978

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference T8465662WO	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 00/ 00217	International filing date (day/month/year) 03/03/2000	(Earliest) Priority Date (day/month/year) 04/03/1999
Applicant NORTRAN PHARMACEUTICALS INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

AMINOCYCLOALKYL CINNAMIDE COMPOUNDS FOR ARRHYTHMIA AND AS ANALGESICS AND ANESTHETICS

5. With regard to the abstract,

the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 00/00217

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims

11,13,15,17,19,21,23,25,27,29,31,33,35,37,39,41,43,45,47,49,51,53,55,57, 59,61,63,65,67,69,71,73,75,77,79,81,83,85 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

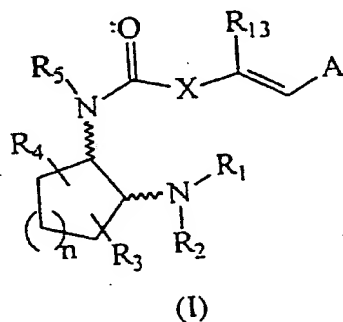
Present claims 1 and 3-89 relate to an extremely large number of possible compounds/methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds/methods where X is a direct bond (as is found in all of the exemplified compounds)

One reason for the limitation is due to the ambiguity as to what is really claimed. It is noted, from the description, but not the claims, that aryl is not meant to have the standard meaning given to it by IUPAC. Not only are non standard meanings (e.g. heteroaromatic) intended, but also the term "optionally substituted" with no limitation as to the type and amount of substitution. The term "optionally substituted" is not allowed for the reasons given in the first 2 sentences of this paragraph. It is further noted that there are no examples of "aryl" being other than phenyl. On page 13, line 22 naphthyl is also referred to which falls within the classic definition of aryl. Accordingly aryl has been understood to only refer to phenyl and naphthyl.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Aminocycloalkyl cinnamide compounds (I) are disclosed. The compounds of the present invention may be incorporated in compositions and kits. The present invention also discloses a variety of *in vitro* and *in vivo* uses for the compounds and compositions, including the treatment of arrhythmia and the production of local analgesia and anesthesia.



$n = 1 - 4$

$R_1, R_2, R_3, R_4, R_5, R_{13}, X$ and A are as in claim 1

INTERNATIONAL SEARCH REPORT

International Application No

CA 00/00217

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D207/09 A61K31/40 C07D295/12 A61K31/535 A61P9/06
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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

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Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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A ✓	US 5 506 257 A (MACLEOD BERNARD A ET AL) 9 April 1996 (1996-04-09) claim 1	1-89
A ✓	WO 93 19056 A (UNIV BRITISH COLUMBIA) 30 September 1993 (1993-09-30)	1-89
	-/--	

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☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
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- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

19 June 2000

Date of mailing of the international search report

10. 07. 00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Gettins, M

INTERNATIONAL SEARCH REPORT

International Application No

CA 00/00217

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	✓ US 5 051 428 A (HORWELL DAVID C ET AL) 24 September 1991 (1991-09-24) claim 1	1-89
A	✓ EP 0 380 063 A (WARNER LAMBERT CO) 1 August 1990 (1990-08-01) claim 1	1-89
A	✓ DE COSTA ET AL: "Synthesis and evaluation of N-substituted cis-N-methyl-2-(1-pyrrolidiny) cyclohexyl amines as high affinity sigma receptor ligands." J.MED.CHEM., vol. 33, no. 11, 1990, pages 3100-3110, XP000910297 example 42; table III	1,2
A	✓ EP 0 222 533 A (UPJOHN CO) 20 May 1987 (1987-05-20) claim 1	1,2
A	✓ US 4 663 343 A (HORWELL DAVID C ET AL) 5 May 1987 (1987-05-05) claims 1,2	1-89
A	✓ US 4 656 182 A (HORWELL DAVID) 7 April 1987 (1987-04-07) claim 1	1-89
A	✓ US 4 598 087 A (HORWELL DAVID C) 1 July 1986 (1986-07-01) claim 1	1-89
A	✓ US 4 179 501 A (SZMUSZKOVICZ JACOB) 18 December 1979 (1979-12-18) claim 1	1-89

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

CA 00/00217

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5506257	A	09-04-1996	AT 154934 T AU 3882793 A CA 2132841 A WO 9319056 A DE 69311896 D DE 69311896 T EP 0632806 A ES 2104142 T HK 1000684 A JP 7505151 T	15-07-1997 21-10-1993 30-09-1993 30-09-1993 07-08-1997 16-10-1997 11-01-1995 01-10-1997 17-04-1998 08-06-1995
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference FB 9564/E14728WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/CA00/00217	International filing date (day/month/year) 03/03/2000	Priority date (day/month/year) 04/03/1999
International Patent Classification (IPC) or national classification and IPC C07D207/09		
Applicant NORTRAN PHARMACEUTICALS INC.et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 04/10/2000	Date of completion of this report 28.02.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Gettins, M Telephone No. +49 89 2399 8273 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00217

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*
Description, pages:

1-51 as originally filed

Claims, No.:

1-89 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00217

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 11,13,15,17,19,21,23,25,27,29,31,33,35,37,39,41,43,45,47,49,51,53,55,57, 59,61,63,65,67 ,69, 71,73,75,77,79,81,83,85.

because:

☒ the said international application, or the said claims Nos. 11,13,15,17,19,21,23,25,27,29,31,33,35,37,39,41,43,45,47,49,51,53,55,57, 59,61,63,65,67 ,69, 71,73,75,77,79,81,83,85 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims -
No: Claims

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00217

Inventive step (IS)	Yes:	Claims	-
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	-
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/00217

- 1). Present claims 1 and 3-89 relate to an extremely large number of possible compounds/methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds/methods where X is a direct bond (as is found in all of the exemplified compounds). It is noted, from the description, but not the claims, that aryl is not meant to have the standard meaning given to it by IUPAC. Not only are non standard meanings (e.g. heteroaromatic) intended, but also the term "optionally substituted" with no limitation as to the type and amount of substitution. The term "optionally substituted" is not allowed for the reasons given in the first 2 sentences of this paragraph. It is further noted that there are no examples of "aryl" being other than phenyl. On page 13, line 22 naphthyl is also referred to which falls within the classic definition of aryl. Accordingly aryl has been understood to only refer to phenyl and naphthyl in terms of the search. The examination has been limited to what was searched.

Since there is no claim which has been fully searched it is not possible to give a clear opinion on novelty, inventive step or industrial applicability on any of the claims in their current form.

- 2). Relevant prior art is provided by:
- (A) EP380063
 - (B) US4179501
 - (C) WO93/19056
 - (D) US4598087
 - (E) US4656182
 - (F) US4663343
 - (G) US5506257
 - (H) J.MED.CHEM, 1990, vol 33, pp3100-3110

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/00217

The Applicant has not explained the reason for the provisos found in claim 1. If they are intended to exclude some unacknowledged prior art known to the Applicant the said prior art should be cited (Rule 5.1 (a) (ii) PCT) and copies of the relevant documents forwarded to the Examiner.

- 3). The current application is novel vis-à-vis (H) on account of the proviso and is novel vis-à-vis (A)-(G) primarily on account of the double bond.
- 4). The compounds of the current application are useful as anti-arrhythmic agents and as analgesics. (H) is not relevant for inventive step since it describes sigma receptor ligands. (A)-(G) are relevant for inventive step since they all describe compounds with the ability to act as anti-arrhythmic agents or as analgesics. The structural difference caused by the structural modification is essentially the replacement of an alkyl group (e.g. (C) or a direct bond (e.g. (A) or (B)) or an alkyl bond optionally containing -O- or -S- (e.g. (E)) by an ethylene group. This structural modification means a change to a conjugated system with a reduced structural flexibility on account of the double bond. An inventive step can therefore be acknowledged or claimed matter which actually has the desired activity.

It must be made credible that essentially all of the claimed matter solves the given problem. With the present scope of the claims this is not the case. The expression in the claims "aryl" and derivatives thereof are non-limitative and are therefore not regarded as obvious modifications or equivalents of the examples which have been given in the description. Accordingly, the said expressions should be restricted in this respect to the particular meanings specified in the description e.g. page 13 (Article 6 PCT). It should be borne in mind that only those compounds which are suitable for solving the problem underlying the present application can be claimed.

- 5). Claims 11,13,15,17,19,21,23,25,27,29,31,33,35,37,39,41,43,45,47,49, 51,53,55,57, 59,61,63,65,67 ,69, 71,73,75,77,79,81,83,85 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims (Article 34(4)(a)(i)PCT).

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/CA00/00217

- 6). The reference on page 34 to "not by way of limitation" should be deleted (Art 6 PCT).
- 7). The Applicant has not cited the prior art documents (A)-(H) (Rule 5.1 (a) (ii) PCT).
- 8). Independent claim 2 should refer back to claim 1 (**Article** 6 PCT).

(PCT Rule 61.2)

To:

**Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room 524
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office**

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on: 04 October 2000 (04.10.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

R. E. Stoffel

Telephone No.: (41-22) 338.83.38